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EXAMINER	
BAUSCH, SARAE L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,728	VAN DER KUYL ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,9,12-14,16,17,19,25-30,33 and 35-47* is/are pending in the application.

4a) Of the above claim(s) *7,13,25-28,35-37 and 39-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 9, 12, 14, 16-17, 19, 29-30, 33, 38, 42-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted on 04/11/2006.

Claim Status

2. Currently, claims 1, 3-5, 7, 9, 12-14, 16-17, 19, and 25-30, 33, 35-47 are pending in the instant application. Claims 2, 6, 8, 10-11, 15, 18, 20-25, 31-32, and 34 are cancelled. Claims 7, 13, 25-28, 35-37, and 39-41 have been withdrawn from consideration as being drawn to a nonelected invention. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented, as necessitated by amendment, or are reiterated from the previous office action. Response to arguments follow. This action is FINAL.

Withdrawn Rejections

3. The rejections of claims 19, 33, 34, and 38, under 35 U.S.C. 112, second paragraph, made in section 12 of the previous office action mailed 10/11/2005, is withdrawn in view of the amendment to the claims.

4. The rejections of claim 34, under 35 U.S.C. 112, first paragraph, made in section 14, of the previous office action mailed 10/11/2005, is withdrawn in view of the amendment to the claims.

5. The objection of claims 38, made in section 9, of the previous office action mailed 10/11/2005, is withdrawn in view of the amendment to the claims.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1, 3-5, 9, 19, 29, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a). Claim 1 is rejected as vague and indefinite for the recitation of "counteracting a status of Kaposi's sarcoma tumor cell". It is not clear what the recitation of "counteracting a status of Kaposi's sarcoma tumor cell" encompasses. The term "counteracting a status" in claim 1 is a relative term that renders the claim indefinite. The term "counteracting a status" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

(b). Claim 19 is rejected as vague and indefinite for the recitation of GenBank number XM 016245 and XM 002037. Reference to these GenBank accession number renders the claim indefinite as the sequence in both record has multiple different versions prior to filing of the instant application and it is not clear which one applicant is referring to. In the instant case, XM 016245 has five different versions and XM 002037 has four different version of the sequence.

Claim Rejections - 35 USC § 112 – Written Description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 19 and 44-45 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. It is noted that this rejection was previously presented in section 14 of the office action mailed 10/11/2005 has been re-written to accommodate the amendment to the claims.

Claim 19 is drawn to a method for determining whether an individual possesses a Kaposi's sarcoma tumor cell comprising determining whether a sample comprises expression products of Siglec-1, GenBank number XM 016245 and Tie 1, GenBank number XM 002037. While the specification asserts that a nucleotide sequence of siglec-1 is SEQ ID No. 72 depicted in figure 8 and TIE 1 sequence as SEQ ID No. 81 depicted in figure 17 (see page 7, paragraph 0020), it does not however teach or describe the entire gene that is associated with this acronym or the entire gene that is associated with GenBank accession numbers. For example, page 30, paragraph 87, recites tag015 (SEQ ID No. 72) (Tie 1, GenBank number XM_002037) however this is not a clear definition that tag 15 is SEQ ID No. 72 which is the entire gene of Tie-1 and GenBank accession number XM_002037. The specification does not explicitly define siglec-1 or tie-1. Furthermore, the content of GenBank accession numbers can change with sequences being added and deleted that can alter the sequence. In addition, reliance upon a GenBank accession record does not provide adequate clarity for the claimed invention, as the content and numbering in a GenBank record can change over time as the records can be updated as time

passes. In this case a potential update to the cited GenBank record wherein a revision includes the addition or deletion would result in a complete change in the numbering system. The reliance of an external GenBank sequence for a numbering scheme is similar to a recitation of a trademark as the GenBank accession number does not represent a fixed disclosure of a sequence but instead refers to a record that is constantly able to be updated and modified. In the instant case, there are four versions of sequence listing associated with the GenBank accession number XM_002037 and five versions of sequence listing associated with the GenBank accession number XM_016245. The specification does not provide adequate written description for siglec, XM_016245 or tie-1 GenBank number XM 002037 as the specification does not disclose the sequence of tie-1 or siglec. Based on the lack of written description in the specification, the skilled artisan would not know which sequences fall within the large genus of the sialoadhesin and Tie-1 expression encompassed by the recitation of the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed siglec-1 GenBank number XM 016245, Tie-1, GenBank number XM 002037, regardless of the complexity or simplicity of the method of diagnosing a disease or determining whether an individual possesses a Kaposi's sarcoma tumor cell. Adequate written description requires more

than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Claim Rejections - 35 USC § 112- New Matter

10. Claims 1,3-5, 9, 14, 16-17, 19, 29-30, 33, and 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation of "at least two fold reduction" in amended claim 1, 16, 17, "at least two fold overexpressed" in amended claim 14, 19, 33, and 38 is not supported in the specification and raises the issue of new matter. Applicant assert that basis for this amendment is found in examples 2-7 and table 1-4. However, tables 1-4 and examples 2-7, teach a 2-10 fold increase for tag032 (siglec gene marker) (see table 4) and a 2-5 fold increase for tag015 (tie-1 marker) (see table 3), however none of these cover the entire range of "at least a two fold" increase in Kaposi's sarcoma tumor cells to determine if an individual possesses a tumor cell. The recitation of "at least" encompasses expression levels greater than 5 and 10 that are not described in the specification. Furthermore, the specification does not teach any expression levels in individuals after treatment. There is no support in the specification that two or more fold underexpression is indicative of effective counteracting of Kaposi's sarcoma tumor cells. There is no support in the specification that greater than two fold overexpression indicates Kaposi's sarcoma tumor cells. The specification is limited to tag15 and tag32 with expression value of 2-5 and 2-10, respectively, for the presence of a Kaposi's sarcoma tumor cells. Therefore, the recitation of "at least two fold reduction" in amended claim 1, 16, 17, "at least two fold overexpressed" in amended claim 14, 19, 33, and 38 is not supported in the specification and raises the issue of new matter.

Claim Rejections - 35 USC § 112- Enablement

11. Claims 1,3-5, 9, 12, 14, 16-17, 19, 29-30, 33, 38, and 42-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

and/or use the invention. . It is noted that this rejection was previously presented in section 14 of the office action mailed 10/11/2005 has been re-written to accommodate the amendment to the claims.

12.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims

The claims are broadly drawn to a method of determining efficacy of treatment by a counteracting the status of Kaposi's sarcoma tumor cells by obtaining a sample after initiating treatment and determining whether sample comprises a change of at least fold in level of an expression product of SEQ ID No. 72 and 81. The methods are further drawn to samples comprising blood samples and peripheral blood mononuclear cells obtained within one week and two days of initiating treatment, and expression of SEQ ID No. 72 and 81 is quantified. The claims are further drawn to detecting expression levels of SEQ ID No. 72 of 2-5 fold change and SEQ ID No. 81 of 2-10 fold change. The claims are also drawn to a method of detecting an expression product of SEQ ID No. 72 and 81 comprising obtaining a sample, introducing a

nucleic acid into the sample, and determining whether the nucleic acid hybridizes to the sample and are further drawn to a tumor cell, comprising Kaposi's Sarcoma,. The claims are also drawn to a method of determining the presence of Kaposi's sarcoma cell in an individual by obtaining a sample from the individual and detecting the level of peripheral blood mononuclear expression of SEQ ID No 72 and 81. The claims are also drawn to a method of determining the presence of a Kaposi's sarcoma tumor cell by obtaining a sample from an individual and detecting the level of peripheral blood mononuclear cell expression of SEQ ID No 72 and 81 and by providing a diagnostic kit, obtaining a sample, and quantifying an expression product of SEQ ID No. 72 and 81.

Guidance in the Specification

The specification asserts a change in expression product of a marker gene is indicative for whether a treatment is effective or not by the level of expression, which can be enhanced or reduced. The specification asserts the expression product of the marker gene is preferably quantified and the level of expression product of marker genes can vary from patient to patient (see paragraph 10, page 4). The specification further asserts that a very sensitive expression detection system will typically detect expression product where a less sensitive system detects no expression product and a person of skill in the art is well capable of designing the most appropriate expression detection system to practice this preferred embodiment (see paragraph 10, page 5), however the specification does not teach the most appropriate expression detection system to detect expression of SEQ ID No. 72 and 81. The specification asserts that in a preferred embodiment the tumor comprises Kaposi's sarcoma. The specification asserts that Kaposi's sarcoma is a disease of proliferating blood vessels and is very much suited for

identifying marker genes, preferably SEQ ID No. 72 and 81, involved in angiogenesis (see paragraph 12, page 5). The specification asserts further that angiogenic mechanism causing the lesions of Kaposi's Sarcoma is an interplay of viral and cellular gene expression and is poorly understood in terms of which genes are involved and what controls their expression (see paragraph 13, page 6). Further, the angiogenic proliferation of Kaposi's sarcoma is likely to be universal in angiogenesis and marker genes for angiogenesis are very suitable for determination of whether a treatment of Kaposi's sarcoma is effective (see paragraph 13, page 6).

The specification asserts a method of determining gene expression patterns in Kaposi's Samoa by serial analysis of gene expression (see paragraph 18, page 6). The specification asserts that the use of a nucleic acid comprising a sequence of Seq ID No 72 and 81 can be used as a detection marker for Kaposi's sarcoma. The specification further asserts that it is possible to monitor a specific status of an individual, the presence of a disease, or developing the disease (see paragraph 26, page 10). However, the specification further states the absence of a marker gene in a sample can be indicative for the presence of a disease or for danger of developing the disease (see paragraph 26, page 10) and that a decreasing amount of expression product in samples in a specific time period can indicate – either beneficial or harmful – process. The specification does not give any guidance on how to determine if the presence or absence of the marker genes, SEQ ID No. 72 and 81, is indicative of Kaposi's sarcoma, developing disease Kaposi's sarcoma, counteracting a status of Kaposi's sarcoma tumor cell or not having Kaposi's sarcoma at all or how to determine if the expression amount is beneficial or harmful.

Working Examples

The specification teaches obtaining SAGE libraries of two patients with Kaposi's Sarcoma that were not treated and obtaining SAGE libraries of one patient after 24 hours of chemotherapy treatments and after 48 hours of treatment and determining the expression profiles of the samples (see page 14-16, examples 1-3). The specification teaches determining markers in skin samples of 5 different samples with Kaposi Sarcoma and 2 control samples without Kaposi's Sarcoma (see example 10, page 33 and figure 19). The specification teaches determining gene expression levels of sequences in peripheral blood mononuclear cell sample by taking blood samples of 4 different patients with Kaposi's Sarcoma and two different patients without Kaposi's Sarcoma and analyzing expression levels (see example 11, page 41 and figure 20). However, the specification provides no indication as to whether the results were statistically significant such that the skilled artisan would be able to predictably correlate the results with the presence of a tumor cell, diagnosis of disease, or efficacy of treatment of disease nor does the specification provide any indication of how to determine if treatment counteracts a status of Kaposi's sarcoma tumor cell.

The following are unclear from the teachings in the specification. The specification envisions hypothetical situations where SEQ ID No. 72 and 81 could determine the presence of a Kaposi's sarcoma tumor cell, angiogensis, disease and efficacy of any treatment of a Kaposi's sarcoma tumor cell associated with Kaposi's sarcoma. The specification appears to be conceiving of possible scenarios where the expression level could be either enhanced or decreased and that these results would indicate the presence – or absence – of a Kaposi's sarcoma tumor cell however, it is unclear how one of skill in the art would determine the level of

expression necessary to determine the presence of the Kaposi's sarcoma tumor cell or angiogenesis. Furthermore, the specification does not teach how to diagnose Kaposi's sarcoma by increase in two fold expression of SEQ ID No. 72 and 81. Specifically, the specification does not teach how that change in two fold expression in Seq ID No 72 or 81 would indicate the presence of Kaposi's sarcoma tumor cell. For example, the specification asserts increased expression in two patients with Kaposi's sarcoma tumor. In table 3, the specification asserts a 2-5 fold overexpression of tag 0015, however table 3 asserts that tag 15 has the sequence of seq ID No. 6, but on page 30 tag 015 is associated with SEQ ID No. 72 and table 4 asserts that an 2-10 fold overexpression of tag 0032 and table 4 teaches the tag 0032 is SEQ ID No. 30, however page 33 teaches that tag0032 is SEQ ID No. 81, Siglec-1. It is unclear if tag 15 and tag 30 are SEQ ID No. 6 or 72 or SEQ ID No. 30 or 81. In addition, these teachings do not provide statistically significant data. Further, it is unclear if a change in expression of Seq ID No 72 and 81 would even indicate the presence of a Kaposi's sarcoma tumor cell or how this change would relate to the efficacy of treatment of a Kaposi's sarcoma tumor cell. The specification does not teach how to detect a two fold change in expression SEQ ID No. 72 and 81 that is indicative of Kaposi's sarcoma nor does it teach how to determine if the expression amount of the marker gene which is beneficial or harmful. The specification lacks guidance on how SEQ ID No. 72 and 81, found in the study on Kaposi's sarcoma, are suitable for determining if any treatment is effective and or determining the presence of Kaposi's sarcoma tumor cell. It is unclear how one of skill in the art would design the most appropriate expression detection system to practice this preferred embodiment and assess the efficacy of the results of the embodiments.

The unpredictability of the art and the state of the prior art

There is a large body of knowledge in the prior art related to angiogenesis in general, and their association with tumor identification, as well as drug or therapeutic response. However, the art is highly unpredictable with regard to the angiogenic status of an individual or the routine assessment of the effect of a given treatment on tumor angiogenesis. Post filing art, Ruegg et al. teaches that to date there is no validated laboratory test to determine the angiogenic status of an individual patient and to routinely assess the effect of a given treatment on tumor angiogenesis (Current Molecular Medicine 2003, 3, pp. 673-691, see specifically page 685, 2nd column, 1st paragraph). It is unpredictable whether any such marker would be associated with angiogenesis and accurately determine a disease state, a physiological state, or drug metabolism or response. For example, Ruegg et al. teaches that developing a test is an enormous challenge with far reaching clinical implications and many reputable academic and pharmaceutical research laboratories are currently engaged in such effort. Ruegg et al. teach that developing a marker specific to a tumor vasculature would require identification of a new marker, from four different samples: the angiogenic endothelial cell, the plasma from same patient, endothelial cells from corresponding healthy tissues from same patients and/or healthy donors, and plasma from healthy individuals (see page 685, 2nd column, 2nd paragraph and figure 4). Even in a case where an association between a particular transcription profiles and an angiogenic disorder, Kaposi's Sarcoma (KS), was found to exist, such as with the applicant's own work (van der Kuyl et al., BMC Cancer 2002 2(1):21) of comparing a patient with AIDS-KS and the effectiveness of treatment by determining a mRNA profile after 24 and 48 hours after therapy to two untreated patients, van der Kuyl et al. found that based on genetic expression profiles the libraries of the treated patient after 48 hours were more closely related to patients untreated than

the treated patient after 24 hours (see page 7, 2nd column 1st paragraph), suggesting that the association between transcription profiles, angiogenic disorder, and treatment prognosis is unpredictable. Further, applicant's own post filing art (Cornelissen et al, BMC Cancer 2003 3:7), teaches a study of semi-quantative PCR analysis of six genes profiles that were found to have increased expression in KS tissue samples and found only one of the six gene expressions had a $P<0.05$ compared to normal skin tissue (see page 9, 1st column, 1st full paragraph and figure 3). Further, figure 3 shows that the other five gene expression profiles of the KS tissue samples are within error of the normal skin tissue samples (see Figure 3, page 12). Cornelissen et al. specifically teaches that it is unpredictable to determine based on gene expression of KS samples an association between angiogenic disorder, diagnosis, and treatment efficacy since Cornelissen et al. shows that normal tissue samples are within error of KS tissue samples. Additionally, van der Kuyl et al. shows a difference in gene expression profiles after 24 and 48 hours after treatment of the same patient, which indicates the unpredictability of determining if a treatment will be effective based on gene expression.

In the instant case, the specification appears to envision scenarios where SEQ ID No. 72 and 81 and parts and analogues expression levels could be used to indicate the presence – or absence – of a Kaposi sarcoma tumor cell, angiogenesis, or any disease. It is unclear how one of skill in the art would determine the level of expression or what part or analogues of SEQ ID No. 72 and 81 would be necessary to determine the presence of the Kaposi sarcoma tumor cell, efficacy of treatment, angiogensis, or diagnosis of any disease considering the unpredictably of the art. The prior art, along with applicant's own post filing art, supports the unpredictability of this area of technology.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Quantity of Experimentation

Given the lack of guidance in the specification with regard to the determining the amount of change in expression of SEQ ID No. 72 and 81, to determine the presence of a Kaposi's sarcoma tumor cell, efficacy of treatment, and relation of the marker genes to angiogenesis in any individual or diagnosis of any disease, and along with the evidence in the art with regard to the variance of determining treatment efficacy by gene expression specifically for angiogenesis, the quantity of experimentation in this area is extremely large. The skilled artisan would have to perform an extremely large study in different populations to determine if in fact there was either an association between SEQ ID No. 72 and 81, siglec-1 or tie-1 would be present in individuals with Kaposi's Sarcoma or any other angiogenic disease relative to individuals without any angiogenic disease. The results of such a study are completely unpredictable as evidence by the evidence presented in applicant's own post filing date art (which reflects the current state of the art) with regard to the gene expression profile of a Kaposi's Sarcoma patient to comparison of normal gene expression profile without the disorder and the variance in expression levels after treatment. Further, post filing art Ruegg et al. teach developing a test to determine the angiogenic status of an individual is an enormous challenge (see Figure 4). The claims are broadly drawn to method of determining efficacy of treatment in a Kaposi's sarcoma tumor cell, determining whether an individual possesses angiogenesis and diagnosing the presence of any disease. To practice the invention as broadly as it is claimed, the skilled artisan would have to determine that SEQ ID No. 72 and 81, tie-1 and siglec would be specific for the Kaposi's

sarcoma tumor cell and determine how much expression would be associated with Kaposi's sarcoma tumor cell to determine if the individual would posses the Kaposi's sarcoma tumor cell. Further, the skilled artisan would have to determine the change in expression values to assess the efficacy of treatment on the Kaposi sarcoma tumor cell. Such experiments are unpredictable, as evidence by the post filing date art and require extensive experimentation and a large research study with a large sample size. The skilled artisan would have to screen each gene profile expression to determine those that possess a Kaposi sarcoma tumor cell in all populations. The skilled artisan would have to perform an extremely large amount of trial and error analysis in a large study to determine if such expression profiles would predictably determine a susceptibility or diagnosis to a Kaposi sarcoma tumor cell or angiogenesis. The skilled artisan would have to perform undue experimentation to determine which Sigel-1 or Tie-1 gene would be predictably correlated to diagnosis of Kaposi's sarcoma tumor cell. Given the lack of guidance in the specification and the conflicting evidence in the art, such analysis is replete with unpredictable experimentation and is considered undue.

Response to Arguments

13. The response traverses the rejection on page 12-13 of the response mailed 04/11/2005. The response asserts that claims, as amended recite how much change in expression level of SEQ ID No. 72 and 81 indicate the efficacy of a treatment in counteracting the status of Kaposi's sarcoma tumor cell. This response has been thoroughly reviewed but not found persuasive. The response asserts that examples 2-7 and tables 1-4 support the amendment of the amount of expression level that indicates the efficacy of treatment. It is noted that tables 1-4, demonstrate a 2-5 increase in tag 15 and 2-10 fold increase in tag 32 in two patients that had Kaposi's sarcoma

tumor cell, however none of these tables demonstrate a decrease in expression of SEQ ID No. 72 or 81 upon treatment or demonstrate counteracting the status of Kaposi's sarcoma tumor cell. Furthermore, the data presented in examples 2-7 and table 1-4 does not provide statistically significant results that would allow one of skill in the art to make and use the claimed invention.

14. The response asserts on page 13, that the disclosure contains sufficient information to enable one skilled in the art to make and use the claimed invention because the specific sequences and indicative changes in their expression are provided in the claims little or no experimentation would be required to make and use this invention. This response has been thoroughly reviewed but not found persuasive because the specification does not describe determining whether a treatment is effective in counteracting a status of Kaposi's sarcoma tumor cells. The specification does not predictably correlate any expression levels of SEQ ID No. 72 and 81 with treatment efficacy for counteracting a status of Kaposi's sarcoma tumor cell, regardless if the claims now recite an expression level. As such the disclosure does not enable one of skill in the art to make and use the claimed invention.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Maintained Rejection

Double Patenting

15. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1, 3-5, 9, 12, 14-19, 21, 24, 31-34, and 38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12, 14-28, and 30-33 of copending Application No. 10/310677. This rejection was presented in section 17-18 of the previous office action mailed 10/11/2005 and is maintained for reasons of record.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

18. Applicant's assert on page 13-14 that the claims of the 10/310677 will be amended to remove the non-statutory double patenting rejection or that a terminal disclaimer will be filed. This response has been reviewed. It is noted that the rejection will be maintained until a terminal disclaimer is filed or the claims in application 10/310677 are amended.

Conclusion

19. No claims are allowable.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 10am-7pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Sarae Bausch, PhD
Examiner
Art Unit 1634

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER